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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,017	07/24/2006	Douglas Spencer Millar	066828-0017	7144

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KNOBBE MARTENS OLSON & BEAR LLP  
2040 MAIN STREET  
FOURTEENTH FLOOR  
IRVINE, CA 92614

EXAMINER
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CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

NOTIFICATION DATE	DELIVERY MODE
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06/20/2008

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com  
eOAPilot@kmob.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/543,017	<b>Applicant(s)</b> MILLAR ET AL.	
	<b>Examiner</b> Suryaprabha Chunduru	<b>Art Unit</b> 1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 33-64 is/are pending in the application.
- 4a) Of the above claim(s) 60-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 33-59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 July 2005 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. The Applicants' response to the office action field on April 09, 2008 has been considered and acknowledged.

***Status of the application***

2. Currently claims 33-64 are pending and claims 33-59 are currently under examination. Claims 1-32 were cancelled. Claims 60-64 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group. Applicants' arguments and the amendment have been fully considered and deemed persuasive for the reasons that follow.

***Informalities***

3. The following informalities are noted:

- (i) claim 38 recites ' the method according to claim 5' a cancelled claim.
- (ii) claim 50 recites ' the method according to claim 15' a cancelled claim.
- (iii) claim 43 recites ' the nucleic acid is undergoes an enrichment or selection step', which would have been ' the nucleic acid undergoes an enrichment or selection step'. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 35-36 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 35 recites ‘wherein the natural or artificial derivatives of DNA or RNA are selected from the group consisting of INA, ANA, MNA, PNA, LNA, HNA, CAN and chimeric combinations thereof’, which is unclear and indefinite because the group of derivatives listed are artificial derivatives of DNA or RNA, thus it is not clear how they refer to natural derivatives of DNA or RNA.

B. Claim 38, 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The meets and bounds of the claims are unclear because it is not clear what limitations it refers to since the claims are dependent on a canceled claim 5 and 15 respectively.

C. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 40 recites the limitation "the untreated nucleic acid" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the claim because the independent claim 33, upon which the instant claim depends lacks support for said limitation ‘untreated nucleic acid’ and thus the limitation in claim 41 lacks antecedent basis.

D. Claims 48-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim 48 recites ‘the ligands’. The meets and bounds of the claim are unclear and indefinite because it is unclear what the limitation refers to, that is, does it

refer to detector ligand or capture ligand or both, especially the claim 47 recites that the detector ligand as an INA ligand. Thus it is unclear whether the limitation refers to detector ligand or capture ligand.

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 33-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grigg et al. (US 2004/0086944 A1) in view of Christensen et al. (US 2006/0014144A1).

Grigg et al. teach a method of claim 33, for detecting the presence of a target nucleic acid in a sample comprising

(a) treating a sample containing nucleic acid with an agent that modifies unmethylated cytosine (see page 2, paragraph 0013);

(b) providing to the treated sample a detector ligand (probe) capable of binding to a target region of nucleic acid and allowing sufficient time for the detector to bind to the target nucleic acid (see page 2, paragraph 0014) and

(c) detecting the binding of the detector ligand to the nucleic acid molecule in the sample as an indication of the presence of the target (see page 2, paragraph 0015).

With regard to claim 34, 36, Grigg et al. teach that the nucleic acid is obtained from genomic DNA (see page 3, paragraphs 0043-0047).

With regard to claims 37-38, Grigg et al. teach that the agent is sodium bisulfite (see page 3, paragraph 0040-0041).

With regard to claims 41-42, Grigg et al. teach that the detector ligand is directed to a CpG containing region which includes a regulatory or enhancer region or promoter region (see page 3, paragraph 0042).

With regard to claims 43-45, Grigg et al. teach that prior to treating the sample, the nucleic acid undergoes an enrichment step that comprises restriction digestion and chemical and antibody treatment to isolate DNA (see page 13, paragraphs 0268-0275, page 7, paragraph 0125).

With regard to claims 47-49, Grigg et al. teach that the method comprises a capture ligand that is bound to a solid support, which is capable of binding to the target nucleic acid, said capture ligand and detector ligand comprises PNA probe (see page 2, paragraph 0023- 0026, 0033, page 3, paragraph 0034, 0045-0046, page 4, paragraph 0049).

With regard to claims 52-54, Grigg et al. teach that the support is selected from a magnetic bead, microtitre plate, bead array, and plurality of capture ligands are arrayed on the solid support (see page 3, paragraph 0036, 0046).

With regard to claims 55-56, Grigg et al. teach that the detector ligand comprises a fluorescent label (see page 4, paragraph 0048).

With regard to claims 57-58, Grigg et al. teach that the nucleic acid bound to the detector ligand is further processed by polymerase chain reaction using primers directed to the regions of nucleic acid (see page 4, paragraph 0061).

However Grigg et al. did not teach use of an intercalating nucleic acid (INA) as a detector ligand or capture ligand.

Christensen et al. teach intercalating nucleic acid ligands and their use in discriminating DNA over RNA, increase specificity of hybridization, increase nuclease stability (see page 2, paragraphs 0024-0034, page 4, paragraph 0072-0083). Christensen et al. also teach that said INA is O-pyrenylmethylglycerol and the target includes chimeric nucleic acid (see page 10, paragraph 0193, 0196); nucleic acids are amplified using PCR and primers comprising INA ligands (see page 120, paragraphs 0958-0962 ).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine or modify the method of detecting the presence of a target nucleic acid in a sample as taught by Grigg et al. with a step of using intercalating nucleic acid ligands as taught by Christensen et al. to achieve expected advantage of developing a sensitive method that can discriminate between DNA and RNA. The ordinary artisan would have motivated to combine the method of Grigg et al. with Christensen et al. because the ordinary

artisan would have reasonable expectation of success that the combination would result in discriminating between RNA and DNA, increase specificity and nuclease stability and decrease cross-hybridization because Christensen et al. explicitly taught that the binding of INA with the target nucleic acid increases the stability of the DNA, inhibit or decrease self and cross-hybridization, discriminate between RNA and DNA and increases specificity (see page 2, paragraphs 0024-0032) and such modification is considered as obvious over cited prior art.

***Response to arguments:***

6. With regard to the objection to the specification, Applicants' arguments and amendment were fully considered and the objection is withdrawn herein in view of the amendment.

7. With regard to the rejection to the claims 33-44 and 55-59 under 35 U.S.C 103(a) as being unpatentable over Eads et al. in view of Christensen et al., Applicants' arguments and the declaration under 37CFR 1.132 by Douglas Spencer Millar, the rejection is withdrawn herein in view of the persuasive arguments and the declaration.

8. With regard to the rejection to the claims 45, and 47-59 under 35 U.S.C 103(a) as being unpatentable over Eads et al. in view of Christensen et al., further in view of Shah et al., Applicants' arguments and the declaration under 37CFR 1.132 by Douglas Spencer Millar, the rejection is withdrawn herein in view of the persuasive arguments and the declaration.

***Conclusion***

No claims are allowable.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Suryaprabha Chunduru/

Primary Examiner, Art Unit 1637